LAMA2-related muscular dystrophy

LAMA2-related muscular dystrophy is a disorder that causes weakness and wasting (atrophy) of muscles used for movement (skeletal muscles). This condition generally appears in one of two ways: as a severe, early-onset type or a milder, late-onset form.

Early-onset *LAMA2*-related muscular dystrophy is apparent at birth or within the first few months of life. It is considered part of a class of muscle disorders called congenital muscular dystrophies and is sometimes called congenital muscular dystrophy type 1A. Affected infants have severe muscle weakness, lack of muscle tone (hypotonia), little spontaneous movement, and joint deformities (contractures). Weakness of the muscles in the face and throat can result in feeding difficulties and an inability to grow and gain weight at the expected rate (failure to thrive). Hypotonia also affects the muscles used for breathing, which causes a weak cry and breathing problems that can lead to frequent, potentially life-threatening lung infections.

As affected children grow, they often develop an abnormal, gradually worsening side-to-side curvature of the spine (scoliosis) and inward curvature of the back (lordosis). Children with early-onset *LAMA2*-related muscular dystrophy usually do not learn to walk unassisted. Speech problems may result from weakness of the facial muscles and tongue, but intelligence is usually normal. Heart problems and seizures occasionally occur in early-onset *LAMA2*-related muscular dystrophy. Because of the serious health problems that occur in this form of the disorder, many affected individuals do not survive past adolescence.

Late-onset *LAMA2*-related muscular dystrophy occurs later in childhood or in adulthood. Signs and symptoms of this form of the disorder are milder than in the early-onset type and are similar to those of a group of muscle disorders classified as limb-girdle muscular dystrophies. In late-onset *LAMA2*-related muscular dystrophy, the muscles most affected are those closest to the body (proximal muscles), specifically the muscles of the shoulders, upper arms, pelvic area, and thighs. Children with late-onset *LAMA2*-related muscular dystrophy sometimes have delayed development of motor skills such as walking, but generally achieve the ability to walk without assistance. Over time, they may develop rigidity of the back, joint contractures, scoliosis, and breathing problems. However, most affected individuals retain the ability to walk and climb stairs, and life expectancy and intelligence are usually not affected in late-onset *LAMA2*-related muscular dystrophy.

Frequency

The prevalence of early-onset *LAMA2*-related muscular dystrophy is estimated at 1 in 30,000 individuals. This condition accounts for between 30 and 40 percent of total

cases of congenital muscular dystrophy, although its contribution may be higher or lower than this range in specific populations. Late-onset *LAMA2*-related muscular dystrophy is rare; its prevalence is unknown.

Genetic Changes

As its name suggests, *LAMA2*-related muscular dystrophy is caused by mutations in the *LAMA2* gene. This gene provides instructions for making a part (subunit) of certain members of a protein family called laminins. Laminin proteins are made of three different subunits called alpha, beta, and gamma. There are several forms of each subunit, and each form is produced from instructions carried by a different gene. The *LAMA2* gene provides instructions for the alpha-2 subunit. This subunit is found in the laminin 2 protein, also known as merosin; it is also part of another laminin protein called laminin 4.

Laminins are found in an intricate lattice of proteins and other molecules that forms in the spaces between cells (the extracellular matrix). Laminin 2 and laminin 4 play a particularly important role in the muscles used for movement (skeletal muscles). The laminins attach (bind) to other proteins in the extracellular matrix and in the membrane of muscle cells, which helps maintain the stability of muscle fibers.

Most *LAMA2* gene mutations that cause the severe, early-onset form of *LAMA2*-related muscular dystrophy result in the absence of functional laminin alpha-2 subunit. Mutations that cause the milder, later-onset form usually result in a reduction (deficiency) of functional laminin alpha-2 subunit. Deficiency or absence of the laminin alpha-2 subunit results in a corresponding lack of laminin 2 and laminin 4, reducing the strength and stability of muscle tissue and leading to the signs and symptoms of *LAMA2*-related muscular dystrophy.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- LAMA2 MD
- laminin alpha 2 deficiency
- laminin alpha-2 deficient muscular dystrophy
- MDC1A
- merosin-deficient muscular dystrophy
- muscular dystrophy due to LAMA2 deficiency

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Congenital muscular dystrophy due to partial LAMA2 deficiency
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1842898/
- Genetic Testing Registry: Merosin deficient congenital muscular dystrophy
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1263858/

Other Diagnosis and Management Resources

- Boston Children's Hospital: Treatment and Care for Muscular Dystrophy
  http://www.childrenshospital.org/conditions-and-treatments/conditions/muscular-dystrophy-md
- GeneReview: LAMA2-Related Muscular Dystrophy
  https://www.ncbi.nlm.nih.gov/books/NBK97333
- Kennedy Krieger Institute: Center for Genetic Muscle Disorders
  https://www.kennedykrieger.org/patient-care/patient-care-centers/center-genetic-muscle-disorders

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Muscular Dystrophy
  https://medlineplus.gov/ency/article/001190.htm
- Health Topic: Muscular Dystrophy
  https://medlineplus.gov/musculardystrophy.html

Genetic and Rare Diseases Information Center

- Congenital muscular dystrophy type 1A
  https://rarediseases.info.nih.gov/diseases/3843/congenital-muscular-dystrophy-type-1a

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Muscular Dystrophy: Hope Through Research
  https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Hope-Through-Research/Muscular-Dystrophy-Hope-Through-Research

Educational Resources

- Centers for Disease Control and Prevention: Muscular Dystrophy
  https://www.cdc.gov/ncbddd/musculardystrophy/
- KidsHealth: Muscular Dystrophy
  http://kidshealth.org/en/parents/muscular-dystrophy.html
- MalaCards: lama2-related muscular dystrophy
  http://www.malacards.org/card/lama2_related_muscular_dystrophy
- Orphanet: Congenital muscular dystrophy type 1A
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=258

Patient Support and Advocacy Resources

- Cure CMD
  http://www.curecmd.org/
- Muscular Dystrophy Association
  https://www.mda.org/
- Muscular Dystrophy UK: Muscular Dystrophies
  http://www.musculardystrophyuk.org/about-muscle-wasting-conditions/muscular-dystrophies/
- National Organization for Rare Disorders (NORD): Congenital Muscular Dystrophy
  https://rarediseases.org/rare-diseases/congenital-muscular-dystrophy/

GeneReviews

- LAMA2-Related Muscular Dystrophy
  https://www.ncbi.nlm.nih.gov/books/NBK97333

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22LAMA2-related+muscular+dystrophy%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28muscular+dystrophy%29+AND+%28lama2%29%29+OR+%28merosin-deficient%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- MUSCULAR DYSTROPHY, CONGENITAL MEROSIN-DEFICIENT, 1A
  http://omim.org/entry/607855

Sources for This Summary

- Allamand V, Guicheney P. Merosin-deficient congenital muscular dystrophy, autosomal recessive (MDC1A, MIM#156225, LAMA2 gene coding for alpha2 chain of laminin). Eur J Hum Genet. 2002 Feb;10(2):91-4.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11938437
- Gavassini BF, Carboni N, Nielsen JE, Danielsen ER, Thomsen C, Svenstrup K, Bello L, Maioli MA, Marrosu G, Ticca AF, Mura M, Marrosu MG, Soraru G, Angelini C, Vissing J, Pegoraro E. Clinical and molecular characterization of limb-girdle muscular dystrophy due to LAMA2 mutations. Muscle Nerve. 2011 Nov;44(5):703-9. doi: 10.1002/mus.22132. Epub 2011 Sep 26.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21953594
- Geranmayeh F, Clement E, Feng LH, Sewry C, Pagan J, Mein R, Abbs S, Brueton L, Childs AM, Jungbluth H, De Goede CG, Lynch B, Lin JP, Chow G, Sousa Cd, O'Mahony O, Majumdar A, Straub V, Bushby K, Muntoni F. Genotype-phenotype correlation in a large population of muscular dystrophy patients with LAMA2 mutations. Neuromuscul Disord. 2010 Apr;20(4):241-50. doi: 10.1016/j.nmd.2010.02.001. Epub 2010 Mar 6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20207543
- Jones KJ, Morgan G, Johnston H, Tobias V, Ouvrier RA, Wilkinson I, North KN. The expanding phenotype of laminin alpha2 chain (merosin) abnormalities: case series and review. J Med Genet. 2001 Oct;38(10):649-57. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11584042
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1734735/
- Miyagoe-Suzuki Y, Nakagawa M, Takeda S. Merosin and congenital muscular dystrophy. Microsc Res Tech. 2000 Feb 1-15;48(3-4):181-91. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10679965

- Reed UC. Congenital muscular dystrophy. Part I: a review of phenotypical and diagnostic aspects. Arq Neuropsiquiatr. 2009 Mar;67(1):144-68. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19330236
- Reed UC. Congenital muscular dystrophy. Part II: a review of pathogenesis and therapeutic perspectives. Arq Neuropsiquiatr. 2009 Jun;67(2A):343-62. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19547838

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